



ARTIFICIAL INTELLIGENCE-DRIVEN MICROBIAL BIOTECHNOLOGY: ADVANCES IN METAGENOMICS, ENZYME ENGINEERING, AND SUSTAINABLE BIOPROCESS OPTIMIZATION

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Received date: 16-04-2026

Accepted date:26-08-2026

Revised date:02-08-2026

Published date:23-09-2026

Abstract

Artificial Intelligence (AI) has become a transformative strategy in microbial biotechnology, offering potential for enhancing microbial identification, functional prediction, enzyme engineering, and optimizing sustainable bioprocesses. This review focuses on the advancements in microbial biotechnology, particularly in the areas of metagenomics, enzyme discovery, and sustainable industrial applications, as influenced by AI. Advances in computational modelling, machine learning and deep learning have enabled more effective identification of microbial communities, functional genes and metabolic pathways, taking the analysis of complex microbial information further. AI can also be used to analyse microbial diversity and discover biologically valuable compounds using metagenomics, or for computational enzyme engineering to predict enzyme functions, substrate specificity, and catalytic properties. Furthermore, AI-driven bioprocess optimization can facilitate optimization of fermentation processes, AI-driven smart monitoring of bioreactors, resource utilization, and sustainable biomanufacturing. However, certain issues around biological data quality, model interpretability, computational load, experimental validation, and industrial applicability remain and further limit the use of these models. The prospect of using new technologies like generative AI, synthetic biology, automated experimentation, and digital twin systems in the field of microbial engineering and process automation is exciting. The future research should focus on robust computational models, bio information standardization, interdisciplinary collaborative applications and applications validated by the experiments. In conclusion, the intersection of AI and microbial biotechnology presents a vast realm of possibilities for discovery, efficiency, sustainability, and responsible application in the biotechnology industry, while also ensuring the responsible integration of technology and ongoing innovation.

Keywords: Artificial Intelligence; Microbial Biotechnology; Metagenomics; Enzyme Engineering; Sustainable Bioprocess Optimization.

1. Introduction

Microbial biotechnology is an important field where solutions to healthcare, agriculture, environmental and industrial problems can be addressed. Microorganisms have a wide variety of metabolic possibilities that make it possible to produce valuable enzymes, pharmaceuticals, bioactive compounds and sustainable bioproducts. The traditional microbial biotechnology relies on laboratory experiments, laboratory identification of microbes and standard molecular techniques, all of which can be time consuming and require considerable expertise and resources. Artificial Intelligence (AI) has ushered in opportunities for improving the efficiency, accuracy and prediction of microbial research. AI tools like machine learning, deep learning, and computational modelling can be used to analyse complex biological data and discover microbial functions and industrial applications (Kumar et al., 2025).

AI has revolutionized the study of microbiology, offering a vast potential for exploring the diversity, metabolic functions, and interactions of microorganisms in complex biological systems. The diversity and complexity of microbial communities challenges traditional approaches for interpretation of large-scale genomic/molecular information. Computational systems using AI can detect patterns, classify microorganisms, make predictions about functional characteristics, and help interpret microbial interactions. These capabilities help in efficient microbial identification, functional characterization and biotechnological development. However, the limitations in the computational prediction rely on the quality of biological information, appropriate model selection, and experimental validation (Srivastava & Mishra, 2025).

The significant value of metagenomics in the field of microbial biotechnology lies in the fact that it can be used to analyse genetic material from environmental and biological samples without the need for cultivating individual microorganisms. The use of machine learning in metagenomic analysis aids in the classification of microorganisms, functional annotation, and identification of potentially valuable genes and metabolic pathways. These techniques enable research into the previously uninvestigated microbial diversity and identification of microorganisms for enzyme production, pharmaceutical development and environmental biotechnology. Genomic data can also be incorporated into machine learning models to predict microbial ecological traits, but there are computational challenges and biological variability to consider (Asnicar et al., 2024).

AI tools in microbial biotechnology have also paved the way to the discovery of natural products and the development of biologically active compounds. Although microorganisms are valuable source of antimicrobial agents, enzymes and other therapeutic molecules, conventional screening methods might fail to identify potentially useful metabolites, or extensive experimental investigation might be required. AI assisted bioprospecting can help prioritize promising microbial candidates, predict biological activities, and identify compounds with potential pharmaceutical applications. These methods can enhance the efficiency of early detection and help to minimize unnecessary experimental screening (Chigozie et al., 2025).

In addition to pharmaceutical discovery, AI applications are now increasingly relevant to sustainable microbial processes and environmental management. Microorganisms are used in degradation and treatment of pollutants, recovery of resources and production of environmentally friendly products. AI-based predictive approaches can be used to select microbial systems, evaluate environmental conditions, and gain insight into factors that impact the performance of bioremediation. In practical application of the technology however, issues such as the variability of the environment, the stability of the microorganisms, and the scalability of the processes need to be taken into consideration. This combination of AI and microbial biotechnology may thus contribute to optimizing environmental remediation processes and resource utilization, promoting sustainable industrial practices (Alavian & Khodabakhshi, 2025). However, issues regarding reliability of the calculations, biological interpretation, experimental validation and industrial application still exist. This review focuses on recent advances in the field of AI for microbial biotechnology, highlighting metagenomics and enzyme engineering, as well as sustainable optimisation in bioprocessing, and reflecting on their challenges and prospects.

Objectives of the Review

- ☐ To examine the applications of artificial intelligence in microbial biotechnology, particularly in metagenomic analysis, microbial identification, and functional prediction.
- ☐ To evaluate recent advances in AI-assisted enzyme discovery, enzyme engineering, and sustainable microbial bioprocess optimization.
- ☐ To identify the major challenges, technological limitations, and future opportunities associated with integrating artificial intelligence into microbial biotechnology.

2. Artificial Intelligence in Microbial Biotechnology

In the field of microbial biotechnology, artificial intelligence (AI) has revolutionized the realm of complex biological information analysis, interpretation, and applications. Microbial identification, functional prediction and discovery of biologically active compounds are supported by machine learning, deep learning, and computational modelling. These technologies facilitate research efficiency and offer potential for pharmaceutical development, environmental biotechnology and industrial use of microorganisms.

2.1. Fundamental AI Approaches in Microbial Biotechnology

Application of Artificial Intelligence techniques in microbial classification, molecular prediction and bioactive compound discovery is rapidly increasing. Machine learning algorithms discover patterns in biological information and deep-learning models process complex genomic sequences, molecular structure and biochemical properties. These are especially useful in pharmaceutical biotechnology to supply a variety of naturally occurring compounds that have potential therapeutic applications. Computational screening with AI support can help identify potential therapeutic targets, predict potential

molecular interactions, and prioritize compounds for experimental testing. Soil microorganisms are significant natural sources of potential anticancer compounds, but their therapeutic efficacy needs to be biologically validated (Albukhari, 2025). The use of AI is also enabling the discovery and characterization of therapeutic peptides. Biological activity and potential toxicity can be predicted by an evaluation of peptide sequences, structural characteristics and physico-chemical properties through computational models. These methods can help to speed up the early stages of drug discovery, avoiding the need for lengthy experimental screening. AI-assisted anticancer peptide discovery showcases the promise of computational technologies in therapeutic molecule discovery and pharmaceutical innovation (Wu et al., 2025).

2.2. Integration of AI with Microbial Omics Technologies

The use of AIOmics technology offers the possibility to study microbial functions and metabolic processes. Biological information, such as genetic composition, gene expression, protein function and metabolic activities, can be obtained from genomics, transcriptomics, proteomics and metabolomics. These molecular components can be related to each other using AI-powered analytical approaches and can help to foretell biosynthetic pathways. Recent progress in metabolic engineering highlights the need to integrate molecular tools with computational strategies to enhance the discovery and synthesis of valuable biological molecules (Injamum-UI-Hoque et al., 2025). Computational integration also has a role in the understanding of how microorganisms interact with environmental or physiological conditions. Microbial communities change in composition and metabolic activity in response to environmental changes. Exposure to heavy metal can affect intestinal microbial communities and their activities, for instance. Biosensor technologies together with computational analysis can help to monitor microbial response and recognize pertinent biological indicators. To accurately interpret, however, reliable measurements and experimental validation are required (Anchidin-Norocel et al., 2025).

2.3. AI-Based Microbial Identification and Functional Prediction

Microbial identification and functional prediction is critical for the discovery of enzymes, metabolites, and compounds of therapeutic value. Traditional methods involve cultivation, biochemical characterization and molecular methods which can be time-consuming and/or inappropriate for microorganisms that are difficult to culture. These methods can be enhanced with AI-driven computational strategies, which predict biological functions and prioritize microbial candidates. The endophytes from medicinal plants are significant reservoirs of natural products with potential therapeutic value, emphasizing the need for enhanced microbial characterization and functional screening (Madagundi et al., 2025). AI-based functional prediction is another way in which it can help the field of antimicrobial compounds. The attention has been paid to antimicrobial peptides for their possible activity against drug-resistant microorganisms. Computational methods can be used to predict the properties of peptides and select those with potential for further investigation. However, experimental studies are still needed to prove antimicrobial efficacy, stability and biological safety. Thus, natural antimicrobial peptides provide promising prospects in combating antimicrobial resistance (Ngashangva et al., 2025). The main computational methods applied in microbial biotechnology, as well as their advantages and disadvantages are listed in Table 1.

Table 1. Major Artificial Intelligence Techniques and Their Applications in Microbial Biotechnology

AI technique or approach	Applications in microbial biotechnology	Major advantages	Limitations	References
Machine learning	Prediction of microbial characteristics and bioactive compound properties	Supports candidate screening and identification of biological patterns	Depends on training information and experimental validation	(Albukhari, 2025)
Deep learning	Prediction of peptide sequences and biological activities	Handles complex molecular relationships and supports therapeutic discovery	Limited interpretability and possible prediction errors	(Wu et al., 2025)
Multi-omics computational integration	Analysis of microbial interactions and biological responses	Combines information from multiple molecular and physiological measurements	Difficulties in data integration and biological interpretation	(Anchidin-Norocel et al., 2025)

Computational functional screening	Identification of bioactive products from microbial endophytes	Supports prioritization of promising natural compounds	Limited characterization of unexplored microorganisms	(Mada gundi et al., 2025)
Sequence-based functional prediction	Identification of potentially useful antimicrobial peptides	Supports identification of candidate therapeutic molecules	Requires experimental evaluation of activity and safety	(Ngash angva et al., 2025)

Overall, AI contributes to microbial biotechnology by improving molecular analysis, microbial characterization, and functional prediction. Its integration with experimental microbiology and omics technologies provides a foundation for further advances in metagenomics, enzyme engineering, and sustainable bioprocess optimization. Figure 1 presents the integrated framework of AI-driven microbial biotechnology, highlighting its major applications and the role of experimental validation. Figure 1 presents the integrated framework of AI-driven microbial biotechnology, highlighting its major applications and the role of experimental validation.

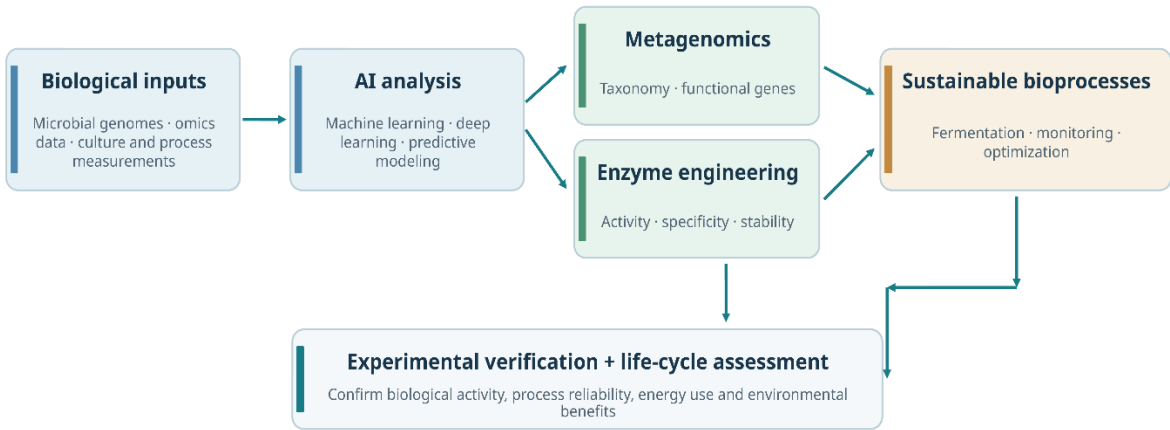


Figure 1. AI-Enabled Microbial Biotechnology: Integrated Framework

3. Advances in AI-Driven Metagenomics

Metagenomics has emerged as a valuable tool for the study of microbial biotechnology without the need for cultures. AI has enhanced the classification of microbes, the prediction of their functions, and the identification of potentially valuable biological resources, when paired with metagenomic technologies. The interpretation of complex sequencing information is supported by machine learning and deep learning approaches, which open new avenues for the discovery of microbes, monitoring the environment, and sustainable biotechnology.

3.1. AI Applications in Metagenomic Sequence Analysis

Metagenomic sequencing yields vast amounts of genetic data, which then needs high level computational tools to accurately interpret. AI-driven methods can aid in the classification of sequences, functional annotation, and the discovery of microbial genes and metabolic pathways. Deep learning models can identify complex sequence patterns and enhance the computational characterization of microbial communities. These methods are especially effective in the study of microorganisms which are still not possible to be identified by traditional cultivation methods. But they can only perform well if the reference databases are good and the training data are well represented, and if the computational resources are adequate. In recent years, deep learning approaches in metagenomics have paved the way for enhancing microbial classification, functional analysis, and the significance of transparent, reproducible computational tools (Roy et al., 2024).

3.2. Microbial Community Profiling and Diversity Assessment

To assess the functions of microbes in natural and engineered settings, there is a need to understand the composition and ecological interactions of the microbial community. AI-powered metagenomic analyses can help profile microbial communities through environmental and functional group analysis as well as diversity analysis. Adding multi-omics data to the computational tool's further views into the microbial metabolic activities and cooperative interactions. Having engineered microbial consortia in environmental biotechnology has been of interest due to the complementary metabolic functions that may be supplied by various microbial populations during the degradation of pollutants. Multi-omics technologies can be integrated with AI to aid in identifying and optimizing microbial communities for xenobiotic bioremediation and wastewater treatment (Renganathan et al., 2025).

3.3. Functional Metagenomics and Novel Gene Discovery

Functional metagenomics can help in identifying microbial genes, enzymes and metabolic pathways that could be useful in biotechnology. AI-powered prediction tools can help to identify functional traits from genomic sequences and identify microorganisms with potentially useful biodegradation traits. Combination of omics technologies with predictive models could be useful for better determination of microbial pathways involved in xenobiotic transformation, pollutant removal and resource recovery. These strategies can be used to create environmentally sustainable microbial systems and circular bioeconomy applications (Renganathan & Gaysina, 2025). Table 2 summarizes the use of AI and related computational methods in metagenomic analysis, functional prediction of microorganisms and environmental biotechnology.

Table 2. Applications of Artificial Intelligence in Metagenomic Analysis and Microbial Functional Prediction

Application area	AI or computational approach	Primary function	Potential biotechnological significance	References
Metagenomic sequence analysis	Deep learning and sequence classification	Microbial identification and functional annotation	Supports investigation of complex microbial communities	(Roy et al., 2024)
Microbial community characterization	Multi-omics integration and AI-assisted analysis	Identification of microbial interactions and functional groups	Supports engineered microbial consortia for environmental applications	(Renganathan et al., 2025)
Environmental functional analysis	Omics-based predictive modeling	Identification of xenobiotic degradation pathways	Supports wastewater treatment and circular resource recovery	(Renganathan & Gaysina, 2025)
Microbial biosynthetic potential	Genome analysis and metabolic modeling	Prediction of vitamin B12 biosynthesis capabilities	Supports selection of promising microbial production systems	(Nelliyan et al., 2025)
Environmental microbial biotechnology	Microbial characterization and process analysis	Assessment of microbial capabilities in wastewater reclamation	Supports development of sustainable treatment processes	(Kumar & Verma, 2025)

Computational methods also play a role in the discovery of microbial biosynthetic capability and the optimization of valuable biological products. The use of genome-based analysis, metabolic pathway reconstruction, and predictive modelling can help in elucidating the different pathways in microorganisms that contribute to the synthesis of vitamins and metabolites. A computational analysis of vitamin B12 biosynthesis identified potential targets for microbial production and potential microbial strains. But the biosynthetic potential of the microorganisms predicted by computation should be verified through experiments before being applied to industry (Nelliyan et al., 2025). The major stages of AI-assisted metagenomic analysis, from sequence generation to functional prediction and biological validation, are illustrated in Figure 2.

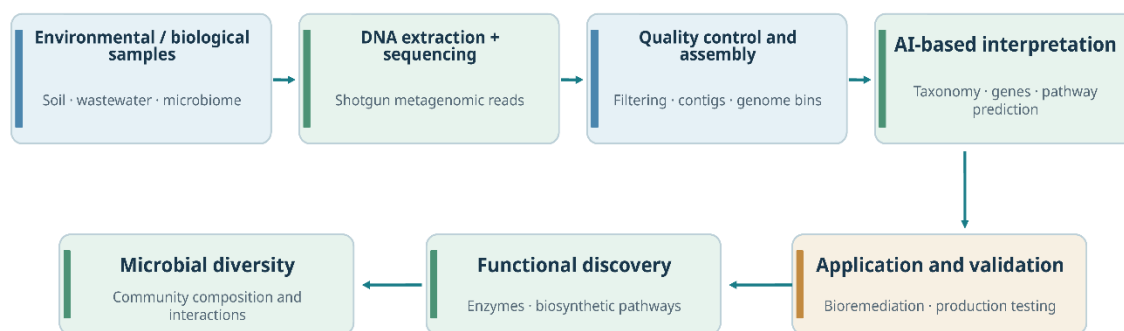


Figure 2. AI-Driven Metagenomic Analysis Workflow

3.4. Challenges in AI-Based Metagenomic Analysis

Incomplete databases and/or biased representation of microbial taxa can influence the functional predictions and classification accuracy. Moreover, even if a gene for a metabolic pathway is found, it does not necessarily mean that it is expressed or active under environmental conditions. These limitations are particularly relevant when it comes to transfer of knowledge from microbial genomes to environmental biotechnology applications. The advances in microbial wastewater reclamation highlight the need to relate molecular characterization to the level of performance, microbial stability and practical operating conditions. Therefore, the combination of computation prediction and experimental validation is essential to gain reliable microbial technologies (Kumar & Verma, 2025). Overall, AI's role in metagenomics is poised for significant expansion, offering a wealth of opportunities for research and development in the field. The computational process, biological validation, and incorporation of multi-omics data will play an important role in future implementation of metagenomic results in biotechnology solutions.

4. Artificial Intelligence in Enzyme Engineering

Enzyme engineering is now an effective application of artificial intelligence (AI) for the discovery, functional prediction and optimization of biocatalyst. To improve enzyme catalytic activity, stability and substrate specificity, considerable experimental trials and several enzyme modifications in the laboratory are usually required in conventional enzyme engineering. The use of AI techniques like machine learning and deep learning, along with protein structure prediction, could accelerate these processes by identifying patterns in enzyme sequences, structures, and biochemical functions. The results can be used as a foundation to produce efficient enzymes that can be used in pharmaceuticals, food processing, biofuel production and environmental biotechnology.

4.1. AI-Assisted Enzyme Discovery and Functional Characterization

Enzyme discovery is required to discover novel biocatalysts with desired biochemical properties. Using AI algorithms, computational methods can be used to analyse protein sequences and structural features to predict the function of enzymes and select targets for experimental testing. Prediction of enzyme functions using deep learning models including structural information have made great progress, particularly in combination with cutting-edge protein structure prediction techniques. Geometric graph learning methods also exploit the structural relationships among proteins, which can help determine potential enzymatic activities and make functional annotation and biocatalyst discovery more efficient. (Song et al., 2024) Structural and functional characterization also provides important clues to the mechanisms of the enzyme and possible applications. Microbial enzymes, such as prepilin peptidase PilD from *Pseudomonas aeruginosa*, are a subject of study that requires investigation of the protein structure, function and biological interactions. The investigations offer valuable experimental data which can be used to characterize enzymes using computational methods and to future predictive modelling. However, the biological relevance of the enzyme functions predicted must be confirmed biochemically and structurally (Dade, 2025).

4.2. Machine Learning for Enzyme Activity and Stability Prediction

Machine learning has broadened the application for the prediction of enzyme properties such as substrate specificity, biochemical capability and catalytic performance. Computational models can be used to find the relationship between protein characteristics and molecular substrates which help in the prediction of enzyme–substrate interaction. These methods might decrease the need for large-scale experimental screening and help to identify enzymes that are appropriate for industrial applications. Machine learning and deep learning models have also proved their potential in predicting small molecule substrates of enzymes and giving useful information for functional annotation or metabolic pathway analysis (Kroll et al., 2023). In addition to substrate prediction, AI can help optimize enzyme stability and activity by identifying sequence variations that are linked to desirable biochemical properties. The use of predictive models can help in prioritizing the enzyme candidates for further testing under different temperature, pH and operation conditions. However, the experiments must be done to verify the prediction, as the performance of an enzyme can vary significantly between biological and industrial applications (Singh et al., 2025).

4.3. AI-Guided Protein Engineering and Enzyme Optimization

AI-guided protein engineering combines computational prediction, rational design and directed evolution to enhance enzyme properties. Machine learning models can assess sequence–function relationships and reveal amino acid substitutions that may be associated with enhanced catalytic activity, stability, and specificity. These methods facilitate the design of functional proteins and minimize the experimental variants to be evaluated in the lab. Advances in protein design using machine learning highlight the transformative power of computing tools in protein modification and the discovery of new useful biological activities (Notin et al., 2024). In addition, advanced enzyme engineering also involves the use of predictive modelling, protein language models and computational structure analysis to identify promising enzyme variants. These technologies have potential to enhance the design of enzymes by identifying promising mutations and testing different combinations of sequence that are hard to test in the lab. Thus, AI can offer the potential of creating tailored biocatalysts with enhanced capabilities for biotechnology applications. Enzyme engineering coupled with microbial strain improvement also plays a crucial role for industrial productivity. The use of biological substrates can be optimized, and valuable products can be synthesized by genetic modifications, optimization of metabolic pathways and enzyme enhancement. The engineering of microbial strains and enzymes is especially significant for the conversion of lignocellulosic biomass, where the ability to degrade and utilize complex plant materials efficiently is crucial for sustainable production processes (Ametefe et al., 2025). Table 3 compares the major AI-assisted methodologies for enzyme discovery, functional prediction, protein engineering and industrial enzyme development. Figure 3 demonstrates the integration of AI-based enzyme prediction, protein modification, experimental testing, and iterative optimization.

Table 3. AI-Based Approaches for Enzyme Discovery, Engineering, and Industrial Applications

Enzyme engineering approach	Major application	Expected benefit	Challenges or limitations	References
Geometric graph learning	Enzyme function prediction using predicted protein structures	Improves computational functional characterization	Dependent on protein structure and model reliability	(Song et al., 2024)
Machine and deep learning	Enzyme–substrate relationship prediction	Supports identification of potential enzyme substrates	Requires representative training information	(Kroll et al., 2023)
Machine learning-guided protein design	Prediction and optimization of protein sequence–function relationships	Supports development of proteins with desired functions	Experimental validation remains necessary	(Notin et al., 2024)
AI-guided enzyme engineering	Prediction of beneficial enzyme modifications	May support improved activity, stability, and specificity	Model generalizability and validation challenges	(Khan & Khan, 2026)
Microbial strain and enzyme engineering	Improvement of biomass conversion and microbial productivity	Supports efficient utilization of biological substrates	Industrial scalability and process variability	(Ametefe et al., 2025)

Ligninolytic enzyme technologies	Biological lignin conversion and valorization	Supports sustainable biomass processing	Catalytic performance and industrial application barriers	(Fu et al., 2025)
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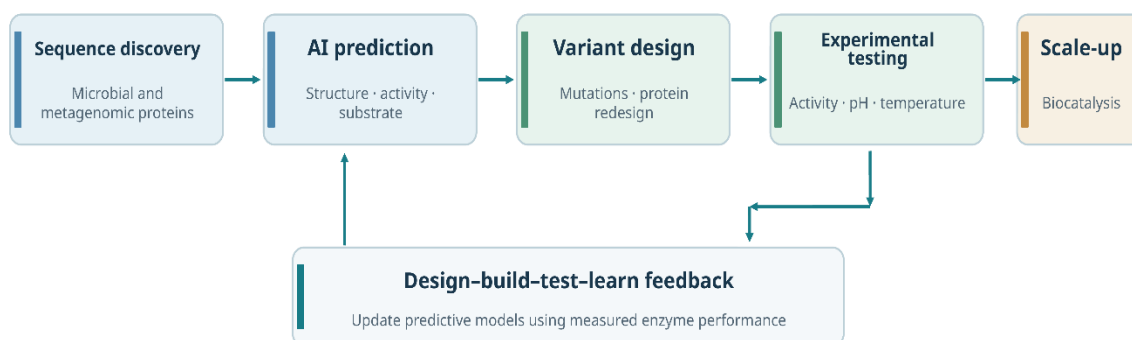


Figure 3. AI-Guided Enzyme Discovery and Engineering

4.4. Industrial Applications of AI-Engineered Enzymes

Enzyme engineering is a key aspect of industrial biotechnology as it helps to develop efficient biocatalysts for biomass conversion, chemical synthesis and environmental applications. Ligninolytic enzymes are especially significant in the conversion of lignin containing biomass materials to useful products. Enzymes can be modified and biological lignin valorisation has improved the utilization of biomass and the reliance on conventional chemical processing. Advancements in AI-assisted methods could also aid in the identification of enzymes with desirable catalytic activity and stability (Fu et al., 2025). The enzymes of the bacteria that break down cellulose and hemicellulose are also of great industrial potential. To produce biofuels, waste valorisation, and sustainable biomanufacturing, cellulases and hemicellulases play a role in the conversion of plant biomass into fermentable sugars and other useful compounds. Enzymes can be discovered and engineered to make them more efficient and enable more cost-effective biomass processing. Bacterial carbohydrate-degrading enzymes are used in a wide range of applications in medical and industrial biotechnology, underscoring their significance (Selim et al., 2025).

In summary, AI can be used to guide enzyme engineering to accelerate functional discovery, enhance enzyme performance, and create industrially relevant biocatalysts. To translate the progress of enzyme design into sustainable applications of biotechnology, computational predictions should be coupled with experimental validation and microbial strain engineering.

5. AI-Driven Sustainable Bioprocess Optimization

Artificial Intelligence (AI) is a key strategy in boosting the efficiency, productivity, and sustainability of microbial bioprocesses. Usually, it takes a lot of experiments to find the right range of operating conditions for microbial growth and product formation in conventional bioprocess optimization. Complex biological interactions can be analysed and decision-making processes optimized using AI-based methods like machine learning, predictive modelling and intelligent process control. These technologies enable the microbial fermentation, monitoring of bioreactors, resource utilization and sustainable production of valuable biological compounds.

5.1. AI Applications in Microbial Fermentation and Bioprocess Monitoring

The production of pharmaceuticals, enzymes, organic acids, biofuels and other industrial bioproducts are widely done by microbial fermentation. These processes are efficient provided microbial growth; availability of substrate, microbial metabolism and operating conditions are met. These relationships can be predicted by AI models and can be used to predict the outcomes of the processes such as the product yield, substrate consumption and fermentation performance. Machine learning methods are also helpful to detect abnormal behavior and deviation of the process early. The combination of predictive modelling and monitoring systems can enhance fermentation consistency, prevent unnecessary experimentation, and facilitate efficient bioprocess management (Mondal et al., 2023).

In addition, computational modelling is useful to monitor microbial processes in food biotechnology. Predictive models can be used to study microbial growth, spoilage behaviour and the effect of environment on microbial activity. These methodologies are useful for food safety evaluation and for designing a monitoring system for microbial contamination. The use of predictive models within food production systems could help make the process more reliable and aid in safer and more efficient industrial processes. Their effectiveness, however, relies on representative observations and validation under practical operating conditions (Qian, 2024).

5.2. Optimization of Bioprocess Parameters Using Machine Learning

Parameters such as temperature, pH, dissolved oxygen, nutrient concentration, and fermentation time must all be carefully considered when optimizing a microbial bioprocess. Traditional optimization strategies often rely on experimental designs to investigate the effect of the factors and their interactions. Factorial statistical designs are systematic ways to identify influential process variables and to examine experimental relationships. These approaches can be combined with AI driven optimization to produce structured experimental data for process improvement and predictive models (Mainardi & Bidoia, 2022).

Machine learning can be used to complement traditional optimization techniques and find nonlinear correlations between several operating parameters and propose appropriate process conditions. AI driven techniques can help optimize the use of substrates, product recovery, energy needs, and process efficiency. They are applied in biorefineries and industrial bioprocessing for process prediction and optimization, and real-time control. AI could then be used to enhance productivity and resource utilization, and to facilitate more sustainable biomanufacturing systems when combined with traditional process engineering (Butean et al., 2025).

5.3. AI-Enabled Bioreactor Control and Process Automation

Monitoring and control of the bioreactor are necessary for proper cultivation of microorganisms and product formation. AI systems can process data from various sensors, predictive models, and automated control strategies, aiding in operational decisions. These can be used to increase the stability of processes, as they are able to detect changes in microbial activity and take corrective action if the process behaviour is predicted to change. Microbial electrolysis cells are an example of complex biological systems where microbial activity needs to be optimized with electrochemical performance. These rely on the process of biofilm formation, electron transfer, availability of substrates and reactor conditions. The challenges in translating microbial biofilm activity into steady electron flow and hydrogen production highlight the need for better process monitoring and control. AI-powered predictive systems could be used to investigate these interactions, though they still need to be further validated to show their practical effectiveness (Mohamed Ashiq et al., 2025).

Combining bioreactor automation with metabolic engineering also offers potential to enhance bio-based chemical production. Engineered microbial pathways can be used to improve substrate conversion and reroute metabolic pathways to create valuable products. These can be complemented with computational modelling and automated process control to determine production conditions that favour and to monitor metabolic performance. This integration could enhance productivity and aid in the creation of efficient microbial manufacturing systems (Mrutyunjaya et al., 2025). The integration of process monitoring, predictive modelling, automated control, and sustainability objectives in microbial bioprocessing is illustrated in Figure 4.

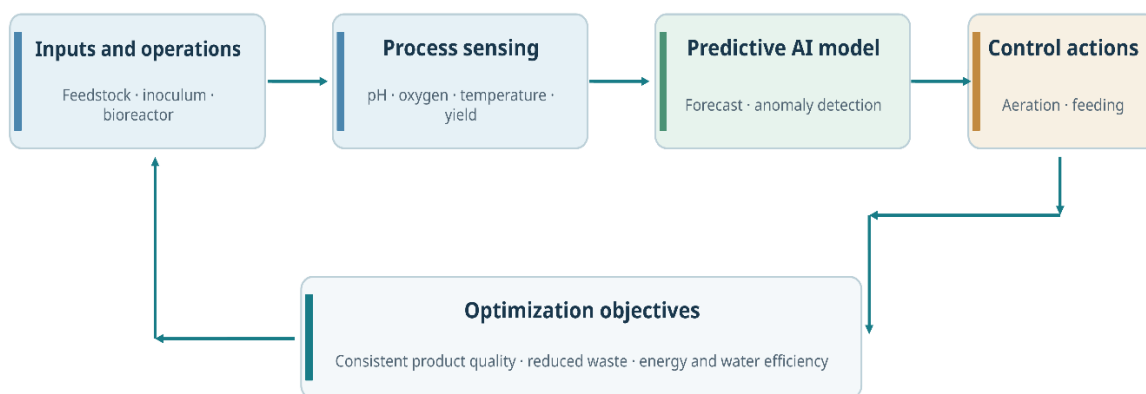


Figure 4. AI-Integrated Sustainable Bioprocess Optimization

5.4. Sustainability and Resource Efficiency in Microbial Bioprocesses

Sustainable bioprocess development involves effective utilization of resources, reduced environmental impact and increased productivity. Microbial systems facilitate the generation of valuable compounds, with renewable substrates. Yeast-based platforms are especially valuable to produce recombinant proteins and bioproducts. AI tools optimize fermentation processes, substrate use and resource management, fostering more sustainable production processes (Belloch-Molina, 2025). Microbial fermentation is also beneficial for sustainable food production, as it enhances nutritional quality and yields valuable metabolites. AI can assist in optimizing the fermentation process, enhancing consistency and improving the quality of plant-based fermented products through predictive modelling (Dhiman et al., 2025). Further opportunities for sustainable biomanufacturing of high value products like vitamins and pigments via microbial production. Engineered microorganisms can be used to transform renewable substrates to valuable and commercial products. The possibility of using metabolically engineered bacteria to produce β -carotene and retinoids may be a viable option, as well as optimizing industrial processes with AI, which could increase productivity (Zhang et al., 2024). Table 4 summarizes the different major approaches that have been used in microbial fermentation, optimization of bioprocesses and sustainable biological production along with their potential benefits and limitations.

Table 4. AI Applications in Sustainable Bioprocess Optimization and Their Potential Benefits

Bioprocess application	Optimization approach	Potential benefits	Major challenges	References
Microbial fermentation	Machine learning-based process prediction and monitoring	Improved operational consistency and productivity	Biological variability and model reliability	(Mondal et al., 2023)
Biorefinery optimization	AI-based predictive modeling and process control	Improved resource efficiency and process management	Integration costs and process complexity	(Butean et al., 2025)
Experimental bioprocess optimization	Factorial statistical experimental design	Identification of influential operating variables and interactions	Requires suitable experimental design and interpretation	(Mainardi & Bidola, 2022)
Microbial electrolysis	Monitoring of biofilm activity and electrochemical performance	Potential improvement in hydrogen production and process stability	Electron transfer limitations and operational challenges	(Mohamed Ashiq et al., 2025)
Sustainable yeast production	Fermentation design and microbial production strategies	Supports production of recombinant proteins and bioproducts	Substrate requirements and production efficiency	(Bell och-Molina, 2025)
Plant-based food fermentation	Microbial fermentation and process improvement	Improved nutritional properties and sustainable food production	Maintaining microbial consistency and product quality	(Dhiman et al., 2025)

Overall, AI-driven bioprocess optimization offers significant opportunities to improve microbial fermentation, operational control, and sustainable industrial production. The integration of predictive modelling, automated monitoring, and metabolic engineering may enhance resource efficiency and product consistency. Nevertheless, reliable industrial implementation requires experimental validation, appropriate process monitoring, and careful consideration of economic and environmental performance.

6. Challenges and Limitations of AI Integration in Microbial Biotechnology

Despite many advances, several challenges remain in the field of artificial intelligence (AI) applications in microbial biotechnology, such as data reliability, computational complexity, biological validation, and industrial implementation. When it comes to microbial identification, AI can be used to improve the process of identifying and engineering enzymes or optimize bioprocesses but requires adequate biological data and experimental support. To address these limitations, accurate, repeatable and industrially feasible AI-enabled microbial tech solutions need to be adopted.

6.1. Data Quality, Availability, and Standardization

AI models rely on biological information quality, diversity, and consistency for their performance in microbial biotechnology. The methods for obtaining the microbial genomic sequences, enzymes characteristics and the fermentation measurements differ, leading to variations in data quality and reporting. Biological annotations were incomplete and imbalanced training samples can result in less accurate prediction and less generalizability of model. Furthermore, there are a few analytical methods that can be standardized and reliable preprocessing methods to fuse information from different life sources. The ability to ensure quality information, suitable computational models and reproducible analytical frameworks is crucial for making reliable scientific predictions, as evidenced in the advancement of chemical and biomedical research using AI (Baranwal et al., 2025).

6.2. Model Interpretability and Biological Validation

A significant challenge is also comprehending the biological significance of predictions made by AI. While complex models based on machine learning and deep learning can make good predictions, understanding underlying biological

mechanisms is lacking. When AI is applied to microbial functions prediction, enzyme activities or metabolic interactions, this is a crucial constraint. Hence, it is necessary to validate the computational results with experiments to ensure its validity and practicality. The dynamic cellular responses, regulatory complexity, and biological variability are other challenges in integrating machine learning with synthetic biological systems. Hybrid quorum sensing/computational-prediction systems show the promise of adaptive biological regulation, but more experimentation and study of system stability is needed to develop them. Importantly, for the development of AI-assisted biological technologies (Tuan et al., 2024), it is essential that predictions by these computational tools are consistent with in situ bacterial behaviour.

6.3. Computational and Industrial Implementation Barriers

Operational and technological issues, that challenge the translation from lab to industry of AI-based microbial biotechnology. Models may be less reliable due to the influence of environmental parameters, variability in substrate and complex biological interactions at the industrial microbial process. In the case of advanced wastewater treatment systems, the focus should be on optimizing the efficiency of combining biological and engineering processes while keeping factors such as operational costs, process complexity, and scalability in mind (Quan et al., 2024). Problems in microbial degradation of plastics are polymer composition, level of microbial activity, environment and low degradation efficiency. AI-assisted approaches can be used for the selection of microorganisms and for process optimization; however, greater experimental testing and industrial feasibility studies are required (Rao & Radha, 2025). Furthermore, the microbial degradation mechanisms, nutrient availability and the environmental stability may differ and influence process performance. To address these challenges, microbial screening needs to be enhanced, process monitoring should be reliable, and biotechnology strategies need to be scalable (Sokra et al., 2025). The current challenges and future perspectives of the use of AI in microbial biotechnology are summarized in Table 5.

Table 5. Major Challenges, Limitations, and Potential Solutions for AI Applications in Microbial Biotechnology

Major challenge	Associated limitation	Potential solution	Expected improvement	References
Data quality and reliability	Incomplete biological information and inconsistent training measurements	Standardized biological information and improved model evaluation	Greater reproducibility and prediction reliability	(Baranwal et al., 2025)
Biological system complexity	Dynamic cellular responses and difficulty predicting biological regulation	Integration of experimental validation with computational modeling	Improved reliability of predictive biological systems	(Tuan et al., 2024)
Industrial process complexity	Variable operating conditions and high treatment requirements	Improved process integration, monitoring, and optimization	Greater operational stability and technological feasibility	(Quan et al., 2024)
Microbial degradation efficiency	Variable plastic composition and restricted biodegradation performance	Improved microbial selection and process optimization	Potentially improved polymer degradation and upcycling	(Rao & Radha, 2025)

Large-scale implementation	Environmental variability and inconsistent microbial performance	Pilot-scale validation, process monitoring, and microbial screening	Improved practical applicability of biodegradation technologies	(Sokra et al., 2025)
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7. Emerging Trends and Future Perspectives

The future of microbial biotechnology with artificial intelligence (AI) will involve greater integration of high-level computational technologies, synthetic biology and automated bioprocess systems. With the emergence of the generative AI, biological foundation models and predictive analytics, opportunities for improved microbial identification, enzyme discovery and metabolic pathway optimization exist. The technologies could accelerate the process of developing industrially relevant microorganisms or in experimental planning and/or prediction in biological studies based on molecular information.

Agentic AI is a new paradigm where computational systems can handle sequential analytical tasks, decipher biological data, and provide varying levels of autonomy to research decisions. These systems can be coupled with microbial biotechnology for better genome analysis, enzyme engineering and identification of potential applications in biotechnology. However, for reliable implementation, human supervision, openness in the AI calculation methods, and experimental testing of the AI-generated predictions (Alaa et al., 2025) are crucial.

The intersection of AI and synthetic biology and automated experimentation may also have a big impact on microbial engineering. Strains, metabolic routes and biological production systems can be improved using AI-driven design – build – test – learn cycles. Automated laboratories and high throughput screening technologies could further speed the determination of microbial functions and properties of enzyme molecules, decrease the experimental time and improve the research efficiencies.

In the future, sustainable biomanufacturing may be further advanced with the use of AI-powered digital twins, smart bioreactors, and real-time optimization of processes. These technologies can support improved monitoring of the fermentation process, prediction of process changes and better use of the renewable resources. The computational reliability, economic feasibility, biological safety and environmental sustainability however would be key factors to a successful industrial adoption. Collaboration between disciplines and experimental validation will still be essential to turn the new AI technologies into real applications on microbial biotechnology.

8. Conclusion

AI has shown potential to revolutionize microbial biotechnology by enhancing microbial characterization, functional prediction, engineering, and sustainable optimization of bioprocesses. The use of machine learning, deep learning, and advanced computational methods to speed up studies of microorganisms and enhance their applications in biotechnology is emphasized. AI-powered metagenomics can be used to discover microbial communities, functional genes, and metabolic pathways, offering insights into microbial diversity and potential. In the same way, AI can help in discovering enzymes, predicting enzyme functions, and developing efficient biocatalysts for industrial and environmental purposes. The potential of AI in microbial fermentation and bioprocess management extends to its impact on productivity, optimal operating conditions, resource utilisation, and sustainable biomanufacturing. However, there are several limitations such as lack of uniformity in biological data, lack of interpretability of models, computational complexity and challenges in transferring the laboratory data to the industry. Experimental validation, standard analytical methods and science-to-science interactions will be needed to overcome these limitations. New technologies like generative AI and synthetic biology, automated experimentation and intelligent bioreactor systems further show potential to support microbial biotechnology and enhance predictive capabilities and process efficiency. The focus of future research should be on the interpretable AI models, scalable bioprocesses, and applications with environmental responsibility. Overall, AI in microbial biotechnology holds significant promise for scientific research, industrial innovation, and sustainable biological production, but it also faces its own set of challenges, such as the need for biological validation of computational predictions and the development of strategies for practical implementation.

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